Remarks/Arguments

Favorable consideration of this application is respectfully requested in view of the foregoing amendment and the following remarks.

Amended Oath

The Examiner has objected to the previously submitted oath because the filing date for the priority document, 60/460,245, is inaccurate. The Applicants are preparing a new oath and will resubmit when completed.

Amendment to the Specification

The Examiner has objected to the disclosure because is contains an embedded hyperlink. The replacement paragraph has deleted the hyperlink. No new matter has been added.

Amendment to the Claims

Claims 1-15 are pending in the application

Claims 1-4, 8-9 are Cancelled, Claims 5, 6 and 10-15 are Withdrawn

Claim 7 remains in the application

Claim 7 is amended to include additional features previously presented in examples 8-10 and original claims 7-9.

Claim 16-18 are new and drawn on data previously presented in examples 8-10 and original claims 7-9

No new matter has been added

35 U.S.C. § 112, 1st paragraph

The Examiner has rejected claims 1, 2 and 7-9 under 35 U.S.C. § 112, 1st paragraph.

Claims 1, 2, 8 and 9 have been cancelled.

The Examiner states that the claims are rejected based on a lack of adequate written description and evidence of possession of the claimed genus. The previously presented claims were drawn to methods of screening compounds against an isolated proton-sensing GPCR having at least 20% identity to the polypeptide of SEQ ID NO: 3. The Examiner has also stated that the claimed GPCR polypeptides do not possess any particular conserved structure nor other disclosed distinguishing feature. Applicants disagree and traverse the rejection in view of the amended claims.

Newly amended Claim 7 now limits the claimed invention to methods of screening for a compound that antagonizes or agonizes a GPR4 related polypeptide, where the GPR4 related peptide is encoded by NM_005282, is the polypeptide of SEQ ID NO: 3 or is a polypeptide at

least 95% identical to SEQ ID NO: 3. Thus, the newly amended claims now recite a GPR4 related peptide having expressly recited structure, or having at least 95% conserved structure relative to SEQ ID NO: 3. As such, the claims require that the GPR4 related peptide have a specifically conserved structure, and possess the distinguishing feature of 95% sequence identity to SEQ ID NO: 3. One of skill in the art would be able to clearly envision the structure of a GPR4 related peptide having 95% sequence identity to SEQ ID NO: 3. Moreover, since the specific structural elements that define GPCRs and dictate their function are well know in the art, such as transmembrane domains, extracellular loops, G-protein binding sites, etc., one of skill in the art would be able to reasonably predict modifications to SEQ ID NO: 3 which would be within the scope of 95% identity and still preserve the function of the protein. Thus, given the teachings in the specification combined with the knowledge and skill in the art, one of skill in the art would immediately recognize that Applicants were in possession of the claimed invention, including the claimed genus of polypeptides with 95% identity to SEQ ID NO: 3.

The Examiner has rejected claim 9, (b) because it recites "a labelled competitor." The rejection is rendered moot as claim 9 has been cancelled and the new claims do not recite "a labeled competitor."

In view of the foregoing, applicants request that the rejection be reconsidered and withdrawn.

35 U.S.C. § 112, 2nd paragraph

The Examiner states that claims 1-4 and 7-9 are rejected under 35 U.S.C. § 112, 2nd paragraph, as being indefinite. Claims 1-4 and 8-9 have been cancelled.

The Examiner has rejected the method claims because they recite "a use without any active positive steps delimiting how this use is actually practiced." The Applicants believe that Claim 7 as currently amended overcomes this rejection by providing a method for screening candidate compounds that includes the step of contacting GPR4 related polypeptide with a compound and determining whether said compound is able to increase or decrease a pH-dependant signal generated by said GPR4 related polypeptide, wherein increasing or decreasing the pH-dependent signal is an indication of the candidate compound being an agonist or antagonist.

New Claims 16-18 further limit the currently amended Claim 7 by further describing methods of testing or the functional characteristic of the candidate compound. Support in the specification for the current amendments and new claims can be found in original claims 7-9 and examples 8-10 of the specification.

In view of the foregoing, applicants request that the rejection be reconsidered and withdrawn.

35 U.S.C. § 102 (e)

The Examiner states that Claims 7 and 8 are rejected under 35 U.S.C. 102(e) as anticipated by Yang et al. (US Patent No. 6,919,176 B2). The Examiner states that Yang et al. teach a human G-protein coupled receptor that is 98.7% identical to SEQ ID NO: 3, as well as teaching screening assays for determining inhibitors and activators of the GPCR and, thus, anticipates the claimed invention. Applicants traverse the rejection on the grounds that Yang et al. does not teach each element of the claimed invention.

The amended claims require an assay that determines the increase or decrease of pH-dependent signaling from the recited GPR4 related polypeptide. Support for this amendment can be found in the specification at pages 40-41. Specifically, the specification teaches cAMP formation is dependent on pH shift. The Applicants have disclosed methods for detecting the pH-dependant signal generated by GPR4 related polypeptides in functional assays (e.g.: in a cAMP-dependent luciferase reporter assay acidic conditions produce a high luminescence signal). The Applicants have further shown that the reported receptor ligand SCP does not activate cAMP formation, nor modulates the pH-dependant signal. Yang et al. do not teach the pH-dependency of cAMP formation and is silent regarding the proton-sensing activity of the receptor. Indeed, the instant application is the first disclosure of the proton-sensing function of GPR4. Prior to the instant disclosure, GPR4 was an orphan receptor and the development of functional assays measuring inhibition or activation of GPR4 activation under inducing conditions was not possible, despite the generic disclosure of Yang et al. Therefore, Yang et al. could not have taught the claimed method for determining a pH-dependent signal because Yang et al. did not recognize this as a property of the claimed receptor that could be used as the basis for a screening assay, such as a pH-dependent reporter assay, for example, under a pH shift in acidic buffer, as described in Examples 8-10. Yang et al. does not teach a screening method that includes the step of determining an increase or decrease in pH dependent signaling of a GPR4 related polypeptide and, therefore, does not disclose each limitation of the claimed invention. Accordingly, Yang et al. does not anticipate the amended claims. Applicants therefore request that the rejection be reconsidered and withdrawn.

The Examiner further states that Claims 7-9 are rejected under 35 U.S.C 102(e) as anticipated by Logan et al. (US 2003/0109044 A1). The Examiner states that Logan et al. teach a human G-Protein coupled receptor, 279, which is 98.7% identical to SEQ ID NO: 3, screening assays for identifying modulators that bind to the 279 receptor or have effect on the 279 receptor expression or activity, as well as a cell based assay in which a cell expressing the 279 receptor is contacted with a test compound and the ability of the test compound to modulate the activity of the 279 receptor is determined. The Applicant respectfully disagrees with the rejection in view of the amended claims, on the grounds that Logan et al. do not teach each element of the claimed invention.

As noted above, the amended claims require a screening assay that determines the increase or decrease of pH-dependent signaling. Logan et al. do not teach the pH-dependency

of cAMP formation and is silent regarding the proton-sensing activity of the receptor. Indeed, the instant application is the first disclosure of the proton-sensing function of GPR4. Prior to the instant disclosure, GPR4 was an orphan receptor and the development of functional assays measuring inhibition or activation of GPR4 activation under inducing conditions was not possible, despite the generic disclosure of Logan et al. Therefore, Logan et al. could not have taught the claimed method for determining a pH-dependent signal because Logan et al. did not recognize this as a property of the claimed receptor that could be used as the basis for a screening assay, such as a pH-dependent reporter assay, for example, under a pH shift in acidic buffer, as described in Examples 8-10. Logan et al. does not teach a screening method that includes the step of determining an increase or decrease in pH dependent signaling of a GPR4 related polypeptide and, therefore, does not disclose each limitation of the claimed invention. Accordingly, Logan et al. does not anticipate the amended claims. Applicants therefore request that the rejection be reconsidered and withdrawn. Neither, Yang et al nor Logan et al teach or suggest the biological function of GPR4, which is its pH-dependant signaling.

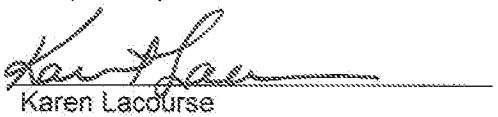
Thus, the Applicants assert that the claimed invention is novel and non-obvious over the cited prior art.

Claim Objection – Minor Informalities

Claims have been limited to SEQ ID NO: 3 and now recites elected subject matter.

Applicants respectfully request that the amendments and remarks made herein be entered and made of record in the file history of the present application. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,



Karen Lacourse
Agent for Applicant
Reg. No. 53,175

Novartis Institutes for Biomedical Research, Inc.
220 Massachusetts Ave.
Cambridge, MA 02139

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